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LETTER

Bullous pemphigoid after inactivated COVID-19 vaccination: Case report

Dear editor,

Vaccination is an effective way to mitigate the current pandemic of Coronavirus disease 2019 (COVID-19) caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[1] Here, we report two cases of bullous pemphigoid (BP) that occurred shortly after COVID-19 vaccination.

Our first case was a 23-year-old man with previous eczema presenting pruritic and tense bullae on the bilateral upper limbs 1 day after receiving a third dose of inactivated COVID-19 vaccine (Changchun Institute of Biological Products Co., Ltd., Changchun, China), spreading over the entire body within 10 days (Figure 1A,B), without response at the site of the first two injections. Histology showed subepidermal blister formation and an inflammatory infiltrate mainly composed of eosinophils in the dermis and bulla cavity (Figure 1C,D). Direct immunofluorescence revealed linear IgG and C3 deposits at the epidermis–dermis junction (Figure 1E,F). Indirect immunofluorescence analysis demonstrated a positive titer of 1:10 for antibasement membrane zone antibodies. Antibodies against BP 180 and BP 230, were 1:32 and 1:10, respectively. Taking into consideration all these findings, a diagnosis of BP was established and the patient was started on intravenous prednisolone at a dosage of 40 mg/day, without new lesions appearing after 7 days.[2,3]

Our second case was an 81-year-old man with hypertension. Injection reaction and blister was not observed after the first two injections. At 15 days after receiving the third dose of inactivated COVID-19 vaccine (Changchun Keygen Biological Products Co., Ltd., Changchun, China), blisters appeared over the entire body with slight itching, continued to develop gradually over a month. Physical examination showed that edematous dark erythema, blisters, blood blisters, and crusts were present on the bilateral upper limbs, groin, and dorsum of the feet, with painful erosion of the oral mucosa and a negative Nikolsky sign (Figure 1G,H). Subepidermal blister, inflammatory infiltrate in the blister and dermis adjacent to the blister, antibodies against BP 180 (1:32), and IgG and C3 deposition at the basement membrane zone supported the diagnosis of BP (Figure 1I–L), therefore, we initiated intravenous prednisolone (60 mg/day) and gamma globulin (20 g/day) therapy, with rapid improvement of all bullae.

BP is the most common autoimmune subepidermal blistering disease of the skin. To date, just about 20 new cases of BP related to the SARS-CoV-2 mRNA-based vaccines produced by Pfizer and Moderna have been reported.[4] To our knowledge, the cases described here represent the first report of BP after administering inactivated COVID-19 vaccine in China. A few cases of BP have been reported with other vaccines, including for swine flu and rabies vaccines, indicating that vaccination can lead basement membrane structure destruction. The current view that circulating Anti-SARS-CoV-2 antibodies do not cross-react with pemphigoid autoantigens does not appear to explain this hypothesis.[5] Recent studies have shown that booster vaccine doses can rapidly evoke a SARS-COV-2 specific immune response.[6] Therefore, it has been suggested that vaccination may induce an enhanced autoimmune response in patients with associated immune predisposition or subclinical BP.[7,8] Reported cases of recurrent BP after vaccination with COVID-19 vaccine may confirm this standpoint.[9] Since BP is most common in the elderly and occasionally in teenagers, we speculate that vaccination may have facilitated the transition from eczema to BP for the first patient, however, the trigger for BP in the second patient remains unclear.

When patients develop blisters after COVID-19 vaccination, dermatologists should consider this possible complication. Existing data show that a relationship between COVID-19 vaccines and BP is uncertain due to the small size of samples. In addition, even if BP is a related adverse event, we do not recommend abandoning the COVID-19 booster vaccine.

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The patients in this manuscript provided written informed consent to the publication of their case details.

CONFLICT OF INTEREST

All the authors disclosed no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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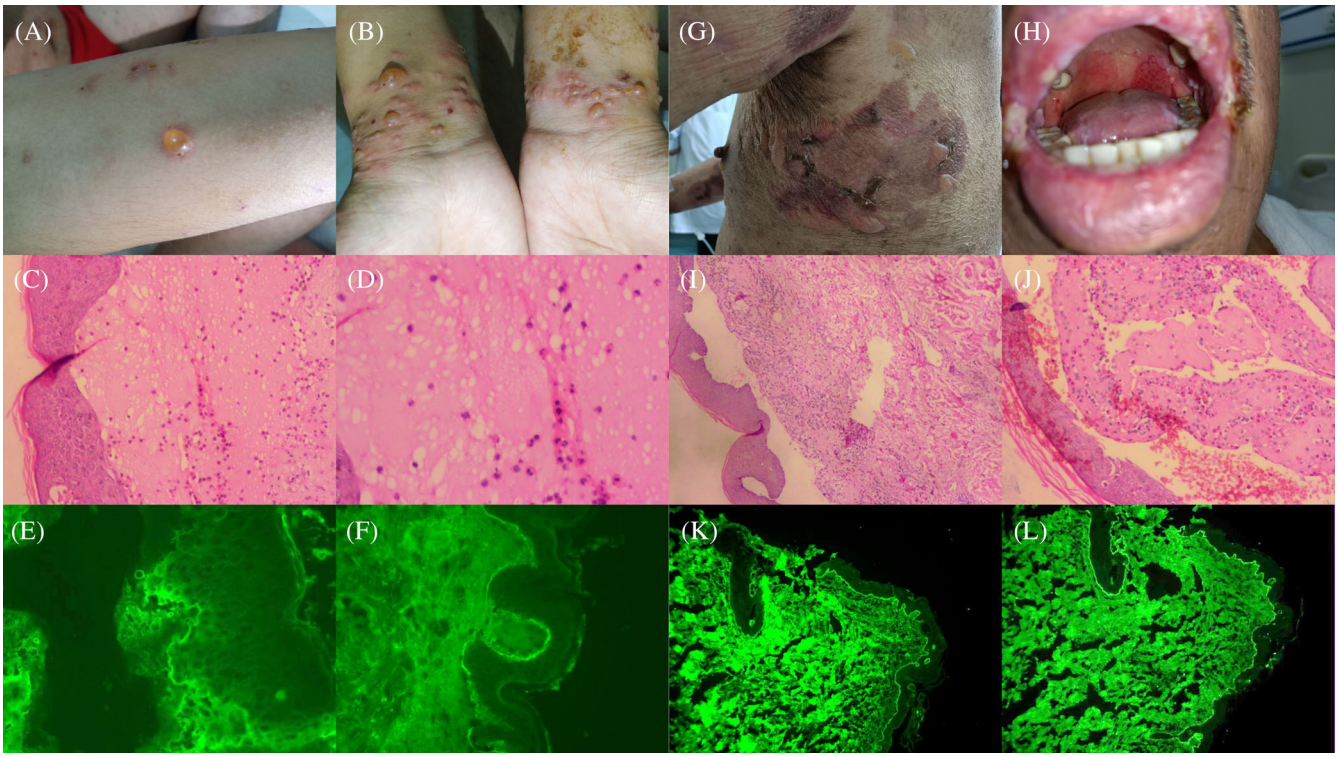

FIGURE 1 (A,B) Blisters, (C) subepidermal bulla (original magnification ×40), (D) eosinophilic infiltration at the epidermis−dermis junction (original magnification ×100), (E,F) Linear basal deposition of IgG and C3, (G) Blisters on the diffuse erythema, (H) oral ulcer, (I) Subepidermal blister (original magnification ×40), (J) inflammatory infiltrate in the blister and dermis adjacent to the blister (original magnification ×100), (K,L) IgG and C3 deposition at the basement membrane zone.

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